Fig. 3 Immunofluorescent localization of human growth hormone. *a*, A section of pancreas from mouse 34-10 treated with rabbit anti-hGH and then with fluorescein isothiocyanate (FITC)-labelled, goat anti-rabbit immunoglobulin. The exocrine acinar cells fluoresce brightly while the endocrine islet cells (arrow) are dark. *b*, A higher magnification view of pancreas from mouse 34-10 demonstrating hGH located in the acinar cells and in a pancreatic duct (arrow). *c*, Pancreas of the same mouse treated with normal rabbit serum before FITC-labelled, goat anti-rabbit immunoglobulin. The arrow indicates islet cells.

Methods. Immediately after the mouse had been killed, the pancreas was dissected and immersed in Carnoy's fixative for at least 2 days. The tissue was embedded in paraffin, sectioned at $\sim 2 \mu\text{m}$ thickness and immunochemically stained, first with either 10% normal rabbit serum or a 1:10 dilution of rabbit anti-hGH serum and then with a 1:50 dilution of FITC labelled, goat anti-rabbit immunoglobulin.

hGH produced by a tissue culture cell line expressing a metallothionein-hGH fusion gene known to give functional hGH (D.M.O. and R.D.P., unpublished data). By this criterion, hGH mRNA seems to be spliced correctly by the mouse exocrine pancreas. Analysis of the same blot using an oligomer specific for pancreatic amylase mRNA demonstrates the pancreas-specific expression of this endogenous gene (Fig. 2*b*). We used amylase mRNA as a control for contamination of other tissues with pancreas (Table 1 legend) and as an internal RNA size marker.

To ascertain whether expression was specific for the exocrine cells of the pancreas, we stained sections of the pancreas with rabbit anti-hGH and fluorescein-labelled goat anti-rabbit immunoglobulin (Fig. 3). The acinar cells of mice expressing the elastase-hGH gene fluoresced brightly, whereas no fluorescence was detectable in the islets of Langerhans (arrows), lymph nodes (not shown), connective tissue and blood vessels (Fig. 3*a*) or in the pancreas of control mice (not shown). The lumen of the pancreatic ducts also fluoresced brightly (arrow, Fig. 3*b*). Substituting normal rabbit serum for anti-hGH serum resulted in no fluorescence (Fig. 3*c*). This analysis suggests that hGH,

an endocrine hormone, can be translated properly and secreted into the gut (where it is biologically ineffective) by pancreatic exocrine cells.

Cellular differentiation follows a genetically defined path leading to the formation of adult tissues. Elucidation of the molecular mechanisms regulating those genes expressed uniquely in terminally differentiated cells will provide insight into the mechanisms guiding the development of a particular tissue. Comparison of the region of the elastase I gene which is sufficient for pancreas-specific expression with comparable regions of other pancreas-specific serine protease genes reveals a conserved 25-nucleotide sequence (Fig. 1*c* and ref. 15). This sequence is included in the chymotrypsin gene constructs that are expressed specifically in pancreatic exocrine cells in culture⁴. The presence of *cis*-acting DNA sequence elements with possible enhancer-like properties^{4,15} implies that regulatory gene products may interact with these elements to control gene expression during development of a particular tissue.

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Corrigendum

Flexure of the continental lithosphere beneath Apennine and Carpathian foredeep basins

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THE vertical force (F) given in Figs 2*b* and 3*b* should be increased by a factor of two to $2.6 \times 10^{15} \text{ dyn cm}^{-1}$ and $3.0 \times 10^{15} \text{ dyn cm}^{-1}$, respectively. The text, p. 144, paragraphs 3 and 4, should be changed accordingly. Thus the applied force is equivalent to a negative buoyancy force generated by a slab with cross-sectional area of 2,600 to 3,000 km^2 in a vertical plane perpendicular to the trench axis. The curves shown in Figs 2 and 3 and the discussion remain otherwise unchanged. This does not change the fundamental results of our study, and, if anything, strengthens the arguments made in the paper—that a subsurface load plays a major role in the formation and maintenance of the Apennine and Carpathian foreland basins. Estimates of the applied vertical force ($2.6\text{--}4.0 \times 10^{15} \text{ dyn cm}^{-1}$) are now in close agreement with estimates of the vertical trench force ($\sim 5 \times 10^{15} \text{ dyn cm}^{-1}$) obtained by Davies²¹.